Screening for Hepatitis C Virus Infection in Adolescents and Adults
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

**Importance**
Hepatitis C virus (HCV) is the most common chronic blood-borne pathogen in the US and a leading cause of complications from chronic liver disease. HCV is associated with more deaths than the top 60 other reportable infectious diseases combined, including HIV. Cases of acute HCV infection have increased approximately 3.8-fold over the last decade because of increasing injection drug use and improved surveillance.

**Objective**
To update its 2013 recommendation, the USPSTF commissioned a review of the evidence on screening for HCV infection in adolescents and adults.

**Population**
This recommendation applies to all asymptomatic adults aged 18 to 79 years without known liver disease.

**Evidence Assessment**
The USPSTF concludes with moderate certainty that screening for HCV infection in adults aged 18 to 79 years has substantial net benefit.

**Recommendation**
The USPSTF recommends screening for HCV infection in adults aged 18 to 79 years. (B recommendation)

The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years. See the Figure for a more detailed summary of the recommendation for clinicians. USPSTF indicates US Preventive Services Task Force.
Assessment of Risk

Although all adults aged 18 to 79 years should be screened, a number of risk factors increase risk. The most important risk factor for HCV infection is past or current injection drug use. In the US, recent increases in HCV incidence have predominantly been among young persons who inject drugs (PWID). Approximately one-third of PWID aged 18 to 30 years are infected with HCV, and 70% to 90% of older PWID are infected. Clinicians may want to consider screening persons younger than 18 years and older than 79 years who are at high risk for infection (eg, those with past or current injection drug use).

Pregnant adults should be screened. HCV prevalence has doubled in women aged 15 to 44 years from 2006 to 2014. From 2011 to 2014, 0.73% of pregnant women tested had an HCV infection, with a 68% increase in the proportion of infants born to HCV-infected mothers. Approximately 1700 infected infants are born annually to 29 000 HCV-infected mothers. Because of the increasing prevalence of HCV in women aged 15 to 44 years and in infants born to HCV-infected mothers, clinicians may want to consider screening pregnant persons younger than 18 years.

Screening Tests

Screening with anti-HCV antibody testing followed by polymerase chain reaction testing for HCV RNA is accurate for identifying patients with chronic HCV infection. Currently, diagnostic evaluations are often performed with various noninvasive tests that have lower risk for harm than liver biopsy for diagnosing fibrosis stage or cirrhosis in persons who screen positive.

Among patients with abnormal results on liver function tests (measurement of aspartate aminotransferase, alanine aminotransferase, or bilirubin levels) who were tested for reasons other than HCV screening, finding the cause of the abnormality often includes testing for HCV infection and is considered case finding rather than screening; therefore, it is outside the scope of this recommendation.

Screening Intervals

Most adults need to be screened only once. Persons with continued risk for HCV infection (eg, PWID) should be screened periodically. There is limited information about the specific screening interval that should occur in persons who continue to be at risk for new HCV infection or how pregnancy changes the need for additional screening.

Screening Implementation

Important considerations for implementation of screening include (1) communicating to patients that screening is voluntary and undertaken only with the patient’s knowledge and understanding that...
HCV screening is planned; (2) informing patients about HCV infection, how it can (and cannot) be acquired, the meaning of positive and negative test results, and the benefits and harms of treatment; and (3) providing patients the opportunity to ask questions and to decline screening.

Some health care systems serving insured populations, some academic medical centers, and the Veterans Health Administration have achieved high rates of HCV screening and treatment. However, national HCV screening rates in community health centers and from the National Health Interview Study were 8.3% and 17.3%, respectively. A study of 4 safety-net primary care practices serving low-income and uninsured or underserved populations found that only 0.8% of persons born in 1945 through 1965 were screened over a 1-year period. Implementation of successful screening may require addressing various barriers to screening and treatment in diverse populations, such as the uninsured.

### Treatment

The purpose of antiviral treatment regimens for HCV infection is to prevent long-term health complications of chronic HCV infection (eg, cirrhosis, liver failure, and hepatocellular carcinoma).

Currently, all oral direct-acting antiviral (DAA) regimens without interferon have been accepted as the standard treatment for chronic HCV infection. Antiviral therapy is not generally considered during pregnancy because of the lack of data on the safety of newer DAA regimens during pregnancy and breastfeeding.

### Additional Tools and Resources

The Centers for Disease Control and Prevention provides strategies for implementing a testing program and additional risk factors at [https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm](https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm).

### Other Related USPSTF Recommendations

The USPSTF has made recommendations on screening for hepatitis B virus infection in pregnant persons, screening for hepatitis B virus infection in adults, and screening for HIV infection.

### Update of Previous USPSTF Recommendation

This recommendation incorporates new evidence and replaces the 2013 USPSTF recommendation, which recommended screening for HCV infection in persons at high risk for infection and 1-time screening in adults born between 1945 and 1965 (B recommendation). The new USPSTF recommendation expands the ages for screening to all adults from 18 to 79 years.

The treatment of HCV continues to evolve, resulting in greater benefits and fewer harms than when the USPSTF last considered the evidence. Direct-acting antiviral regimens are of shorter duration, with higher rates of sustained virologic response (SVR) and fewer serious harms than previous treatment regimens. Since 2013, the prevalence of HCV infection has increased in younger persons aged 20 to 39 years. There are limited epidemiologic data available on HCV incidence in adolescents younger than 18 years. The HCV infection prevalence rates in older adults born between 1945 and 1965 remain relatively high, and prevalence in the elderly will increase as this population ages. Clinical trials of DAA treatment included adults in their early 80s, which increases the evidence for the benefits of screening in older adults. In addition, many older adults could experience the benefits of screening. As a result, the USPSTF concluded that broadening the age for HCV screening beyond its previous recommendation will identify infected patients at earlier stages of disease who could greatly benefit from effective treatment before developing complications.

### Supporting Evidence

#### Scope of Review

The USPSTF commissioned a systematic evidence review to update its prior review (from 2013) on screening for HCV infection. The scope of this review is similar to that of the prior systematic review, except in the current review, the USPSTF also examined the...
evidence on adolescents. For treatment, the USPSTF focused on currently recommended DAA regimens.

**Accuracy of Screening Tests and Risk Assessment**

The USPSTF previously found HCV screening to be highly accurate. The USPSTF found no new evidence on the yield of repeat vs 1-time screening or alternative screening strategies (eg, different risk- or prevalence-based methods).

**Benefits of Early Detection or Treatment**

The USPSTF found no direct evidence on the benefits of HCV screening vs no screening on health outcomes or the effects of prenatal HCV screening on the risk of vertical transmission. Treatment studies focused on populations without cirrhosis who are more likely to be asymptomatic and identified by screening. Of the trials of DAA regimens (n = 7167; 26% to 69% female; mean age, 45 to 62 years), 14 were multinational; 11 were conducted in the US or Canada; and the remainder were conducted in New Zealand, Egypt, France, or Asia. In 29 trials, 60% to 100% of patients were white. The trials evaluated a variety of DAA regimens recommended in current guidelines. Treatment duration was 12 weeks in all but 2 trials, which allocated patients to either 8 or 12 weeks of treatment. Eleven trials were of good quality and 22 were of fair quality. Forty-nine trials found DAA regimens to be associated with pooled SVR rates ranging from 95.5% to 98.9% across genotypes. Evidence was greatest for genotype 1 infection (32 trials), the most frequent genotype in individuals who achieve SVR and an estimated 4400 fewer cases of hepatocellular carcinoma over a lifetime.

**Harms of Screening or Treatment**

The USPSTF did not identify any new studies providing direct evidence on screening harms. Poor-quality evidence from the prior review suggested potential negative psychological and social effects from HCV screening.

Direct-acting antiviral regimens are associated with fewer harms than older interferon-containing therapies. Treatment duration has shortened from 24 to 48 weeks with older interferon-containing regimens to 8 to 12 weeks. In DAA trials (33 trials; n = 7167) with adverse event data, the pooled rate of any adverse event was 73.3%. Rates of serious adverse events (1.9%) and withdrawal due to adverse events (0.4%) were low compared with rates reported for interferon-containing regimens. Pooled rates of specific adverse events ranged from 2.4% for anemia to 18.4% for headache and were also lower when compared with rates reported for older interferon-containing therapies. The most common adverse events were fatigue, headache, nausea, and diarrhea.

Seven nonrandomized, open-label trials (n = 300) in adolescents examined treatment harms. Five trials reported no withdrawals due to adverse events; 1 trial reported a serious adverse event (grade 3 joint injury). The rate of any adverse event was 27% in 1 trial and 71% to 84% in 4 trials. Specific adverse event rates across trials ranged from 3% to 48% for headache (7 trials), 5% to 53% for fatigue (7 trials), and 3% to 28% for gastrointestinal adverse events (nausea, vomiting, or diarrhea) (5 trials). Three trials reported no deaths in adolescents (n = 182) treated with DAA regimens. These trials were not designed to evaluate long-term harms associated with DAA treatment during adolescence.

**Response to Public Comment**

A draft version of this recommendation statement was posted for public comment on the USPSTF website from August 27 to
September 23, 2019. Some comments asked for a definition of “high risk”; however, an extensive list of risk factors is beyond the scope of this recommendation statement. The Additional Tools and Resources section provides a link to other resources. Some comments expressed concern about the lack of guidance on screening intervals for pregnant adults. In response, the USPSTF added language about counseling and consent to the Screening Implementation section. Some comments urged more research on the benefits and harms of treatment in pregnant adults. The USPSTF clarified its call for research in pregnant persons in the Research Needs and Gaps section.

Research Needs and Gaps

Addressing several key research gaps could help inform the benefit of screening for HCV infection in US-based populations:

- Research is needed on the yield of repeat vs 1-time screening for HCV and different repeat screening intervals to inform recommendations on optimal screening intervals for persons at high risk.
- Research is needed to identify labor management practices (eg, prolonged rupture of membranes or use of internal fetal monitoring) and treatment of HCV infection prior to pregnancy to reduce the risk of mother-to-child transmission. Research is also needed on the benefits and harms of additional screening during pregnancy for low-risk persons who have been previously screened.
- Trials and cohort studies that measure effects on quality of life, function, and extrahepatic effects of HCV infection (eg, renal function, cardiovascular effects, or diabetes) would be helpful for evaluating the effects of DAA regimens on short-term health outcomes.
- Additional studies are needed to examine the epidemiology of HCV infection and the effectiveness of DAA regimens in adolescents.

Recommendations of Others

The Centers for Disease Control and Prevention is in the process of updating its HCV screening guidelines. Its draft screening guideline recommends screening for HCV at least once in a lifetime for all adults 18 years and older, except in settings where the prevalence is less than 0.1%. All pregnant persons should be screened for HCV during each pregnancy, except in settings where the prevalence of HCV infection is less than 0.1%. All persons with risk factors (eg, persons with HIV, prior recipients of blood transfusions, persons who ever injected drugs and shared needles, and persons who are born to an HCV-infected mother) should be tested for HCV, with periodic testing while risk factors persist.\(^2\) The American College of Obstetricians and Gynecologists recommends offering HCV screening to pregnant persons with risk factors.\(^2\) The American Association for the Study of Liver Diseases and the Infectious Diseases Society of America recommends 1-time routine, opt-out HCV screening for all persons 18 years and older and 1-time testing for all persons younger than 18 years at increased risk of HCV exposure. They also recommend periodic testing for persons with an increased risk of HCV exposure and annual HCV testing for all PWID and for HIV-infected men who have unprotected sex with men.\(^27\)


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